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EXAMINER

KRISHNAN, GANAPATHY

ART UNIT

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1623

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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DETAILED ACTION

The amendment filed 5/28/2008 has been received, entered and carefully considered.

The following information provided in the amendment affects the instant application:

1. Claims 1-12, 21-68 and 82 have been canceled.
 2. Remarks drawn to rejections under 35 USC 103(a).
- Claims 13-20, 69-81 and 83-85 are pending in the case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of Claims 13-20, 69-81 and 83-85 under 35 U.S.C. 103(a) as being unpatentable over Gosselin et al (US 6,444,652, '652 patent) in combination with Weis et al (WO 96/13512), is being maintained for reasons of record.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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Applicants have traversed the rejection arguing that:

1. In sugars where there is a group at C-2, usually an acyl there is neighboring group participation to form an acyloxonium ion, which leads to exclusively the beta nucleoside. Since there is no neighboring group at the C- position in a deoxy sugar the coupling of the silylated nucleobase such as uracil to a deoxyribose produces a mixture of alpha and beta nucleosides. Halo-deoxyribose in solution generally rapidly isomerizes to a mixture of alpha and beta isomers and lead to a mixture of alpha and beta nucleosides. Since riboses and deoxyriboses behave differently in stereoselectivity it is improper to combine the teachings of Weis and Gosselin to arrive at the present invention.

2. The protected ribose sugar 143 in col. 19 in Gosselin is different in structure than the ribose sugar 1 in col. 25-26. The ribose sugar 1 cannot be prepared according to Reaction 1 in col. 19.

3. The Examiner has compared the wrong examples in Weiss. The ribose at page 13 of Weiss has two OTol groups and is a deoxyribose and the sugar at page 9 of Weiss has three OBz and an OAc group. The OBz group in the two position in the sugar at page 9 can sterically shield the 1 position and can slow down the reaction with the silylated base. There are at least four differences between the ribose sugars and one of skill in the art would not have recognized which factor is actually responsible for the decrease in reaction time.

4. According to instant claims 13 or 17 the acid halide is generated from the reaction of an acyl halide and alcohol; sub-equivalent amount of alcohol is used for producing the acyl halide and the acid halide is anhydrous. The prior art does not teach or suggest these.

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Applicants' arguments and the Organic Reactions reference have been considered but are not found to be persuasive.

1. The instant claims are drawn to preparation of beta-L-2'-deoxythymidine. The process of the prior art may also yield the alpha isomer in addition to the beta isomer. The process of the prior art still reads on the instant claims since it produces the required beta nucleoside. The Organic Reactions reference provided by the applicants teaches that halofuranoses undergo gradual isomerization in the presence of a catalyst (page 35, last paragraph through page 36, first paragraph). They do not isomerize rapidly as applicants have argued. Moreover, in the instant process as well as in the process of the prior art, the type of catalyst as taught in the Organic Reactions reference is not used in the step where the silylated base is coupled to the haloribose (see Weiss, page 13). Hence, isomerization of the haloribose will not be rapid and may not even take place to a considerable extent. Weiss teaches the preparation of a beta-L-2'-nucleoside using a similar coupling step (page 13). The instant claims are not drawn to selectivity. It is proper to combine the prior art of record.

2. The reaction scheme at col. 25-26 in Gosslein teaches steps that are recited in instant claim 13(a) and (b) and the reaction 1 at col. 19, teaches the use of an acid scavenger as recited in instant claims 76-77. These are steps that are instantly claimed. The same chemistry can be used by one of skill in the art in a deoxy ribose too. The ribose sugar 1 need not necessarily be prepared according to reaction 1 in col. 19. The protecting groups used are different as is the group at the anomeric carbon. The protecting group can be chosen according to the design of the process by one of skill in the art.

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3. The examples compared in Weiss are not wrong examples. They are relevant to the instant process. The OBz group in the starting sugar at page 9 of Weiss will not sterically shield the 1 position since it is bonded via a single bond to the oxygen and can point away from the 1-position. The aromatic ring in the benzyl group is free to rotate about the C-CH₂- bond and can take up an orientation that poses no steric hindrance. This is common knowledge and is also well known to one of ordinary skill in the art. It also doesn't matter which factor is responsible for the decrease in reaction time. The only relevant point is that the reaction is slow (as taught by Weiss). Hence, based on the teaching of Weiss one of skill in the art would not prefer to have OAc as the substituent at the 1 position when a halogen at the same position is taught to speed up the coupling with the silylated base.

4. How the acid halide is generated and how much reagent is used is not critical. The step of using an acid halide like HCl (which falls under the definition of acid halide) is taught by Weiss (conversion of structure 54 to 55). This is similar to the step instantly claimed. Here again the type of acid halide used is a matter of choice. One of skill in the art would expect the end result to be the same. Applicants have not shown the criticality of the step as instantly claimed. Substituting the HCl taught by Weiss with another source of halogen like an acyl halide is well within the skill level of the artisan.

Conclusion

Claims 13-20, 69-81 and 83-85 are rejected

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THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang, Ph.D./

Supervisory Patent Examiner, Art Unit 1623

GK